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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,872	04/05/2001	Alan Solomon	044137-5029-US	3133

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,872	SOLOMON ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 32-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 32-57* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 1-3 and 32-57 are pending.

Applicants' amendment filed October 25, 2002 (Paper No. 8) is acknowledged. Applicants' response has been fully considered. Claims 4-31 have been cancelled, claims 1-3 have been amended, and new claims 32-57 have been added. Therefore, claims 1-3 and 32-57 are examined.

2. Formal drawings filed October 25, 2002 (Paper No. 9) is acknowledged.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

3. The previous rejection of claims 1-3 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicants' amendment of the claim, and applicants' response at page 6 in Paper No. 8.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 32-52, 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of removing amyloid from a transgenic rapid, inducible amyloid deposition (TRIAD) mouse, comprising administering an immunoglobulin light chain polypeptide (e.g., whole chain or variable domain) to generate an immune response; or, a method of removing amyloid deposits from a patient, comprising

administering amyloid-β peptide or its variants, or a pharmaceutical composition comprising the amyloid-β peptide, its variants, or immunoglobulin light chain polypeptide as indicated in the prior art, does not reasonably provide enablement for a method of removing amyloid deposits from a subject, comprising administering amyloid fibrils to generate an immune response; a pharmaceutical composition comprising the amyloid fibrils. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1-3, 32-52, 56 and 57 are directed to a method of removing amyloid deposits from a subject, comprising administering amyloid fibrils to generate an immune response (claims 1, 2, 32-45, 50-52, 56 and 57); or a pharmaceutical composition comprising the amyloid fibrils (claims 3, 46-49). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention provides a method of removing amyloid deposits from a patient, comprising administering amyloid fibrils to generate an immune response that will promote the removal of in vivo amyloid fibrils (page 10, paragraph 0035). There are no indicia that the present application enables the full scope in view of a method of removing amyloid deposits by administering amyloid fibrils as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the

unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding various amyloid fibrils and the subject, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no other working examples indicating a method of removing amyloid deposits from a patient by administering various amyloid fibrils except for using synthetic fibrils of immunoglobulin light chain to a TRIAD mouse (paragraphs 0128-0131).

(3). The state of the prior art and relative skill of those in the art:

The prior art indicates a method of removing amyloid deposits from a patient by administering amyloid-β peptide or its variants (Kline *et al.*, WO 95/31996; Schenk *et al.*, WO 99/27944), however, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identities of variants of the cited amyloid fibrils (paragraph 0078), the subject, the treating conditions to a subject, and the effects of amyloid fibrils to be considered enabling.

(4). Predictability or unpredictability of the art:

The claims encompass a method of removing amyloid deposits from a subject, comprising administering amyloid fibrils to generate an immune response. However, the specification does not demonstrate the effects of various amyloid fibrils nor the variants thereof to various subjects except for administering an immunoglobulin light chain polypeptide to a

TRIAD mouse. Therefore, the invention is highly unpredictable regarding the outcome of the claimed method.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of removing amyloid deposits from a subject, comprising administering amyloid fibrils to generate an immune response. The specification indicates amyloid fibril encompasses fibrils of immunoglobulin light chain, amyloid A protein, beta 2-microglobulin, transthyretin, cystatin C variant, gelsolin, procalcitonin, PrP protein, amyloid beta-protein, apoA, lysozyme, variants thereof or allelic variants thereof (paragraph 0078). However, the specification has not identified any variant of cited amyloid fibrils, nor demonstrated the use of any cited amyloid fibrils to a subject except for administering an immunoglobulin light chain to a TRIAD mouse. There are no working examples demonstrating the effects of various amyloid fibrils and variants thereof in subjects other than TRIAD mouse. Since the specification fails to provide sufficient teaching on the identities of variants, the treating conditions such as the dose and the effects for various amyloid fibrils to a subject, it is necessary to carry out further experimentation to assess the effects of these amyloid fibrils in a subject.

(6). Nature of the Invention

The scope of the claims encompasses a method of removing amyloid deposits in a subject using amyloid fibrils to generate an immune response to remove the in vivo amyloid deposits, and a pharmaceutical composition comprising amyloid fibrils, but the specification has not

demonstrated the effects of various amyloid fibrils in a subject other than TRAID mouse. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the variants in the method, the art is unpredictable regarding the variants, and the guidance and the teaching in the specification are limited, therefore, it is necessary to have additional guidance/teaching and to carry out further experimentation to assess the effects of these variants in the claimed method.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, 32-45, 50-52, 56 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1, for example, recites the limitation " the patient" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim. See also claim 50 for "the mammal". Claims 2, 32-45, 51-52, 56 and 57 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

7. Claim 37 is indefinite because of the use of the term "cystatin C variant". The term "cystatin C variant" renders the claim indefinite, it is not clear what amino acid sequence is intended as to "cystatin C variant", and how different the variant is as compared to the parent compound.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 3, 32-40, 46, 56 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Kline *et al.* (WO 95/31996).

Kline *et al.* teach a method for alleviating the symptoms of a disease state association with plaque formation such as Alzheimer's disease by administering to a human patient amyloid beta protein or a derivative thereof, which stimulates the appropriate metabolic regulatory system, e.g., immune system such that amyloid plaque developments are slowed, and accumulated proteins are eliminated (page 9, lines 2-7; page 12, lines 19-25; page 13, lines 24-25; Examples; claims 1, 35-40, 56). Amyloid beta protein can be obtained by conventional means known in the art (page 3, lines 5-17; claims 32-34, 57). The reference also teaches a pharmaceutical composition comprising amyloid beta protein and a liquid or solid carrier (page 12, line 28-page 13, line 3; claims 3 and 46).

9. Claims 53 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Ostberg *et al.* (U. S. Patent 5,750,106).

Ostberg *et al.* teach a Pharmaceutical composition for treatment of a cytomegalovirus (CMV) viral infection, the composition comprising a buffer (Examples III and IV) and a human anti-CMV antibody which comprisies a human immunoglobulin heavy chain having a variable

region of SEQ ID NO:3 and a human immunoglobulin light chain having a variable region of SEQ ID NO:3 (claim 6 of U. S. Patent 5,750,106; claims 53 and 54).

10. Claims 1, 3, 32-49, 56 and 57 are rejected under 35 U.S.C. 102(a) as being anticipated by Schenk *et al.* (WO 99/27944).

Schenk *et al.* teach a method for treating patients suffering from amyloidogenic disease such as Alzheimer's disease by administering amyloid-beta peptide (Aβ) or variants thereof to induce immune response against amyloid deposit in the patient (page 3, lines 1-17; page 13, lines 28-33; page 43, line 24-page 45, line 20; claims 1, 35-40, 56), and the PDAPP transgenic mice treated with one Aβ peptide has 81% less total Aβ level at 15 months than the PBS-immunized group (Tables 2-4, page 43, line 24-page 45, line 20; claims 41-45). Aβ, and its fragments, or analogs can be synthesized by solid phase peptide synthesis or recombinant expression, or obtained from natural sources (page 15, lines 24-27; claims 32-34, 57). The reference also teaches a pharmaceutical composition comprising amyloid-beta peptide, a carrier and an adjuvant such as alum (page 4, lines 23-25; page 25, lines 24-32; page 28, lines 28-35; claims 3 and 46-49).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ostberg *et al.* (U. S. Patent 5,750,106) taken with Theofan *et al.* (U. S. Patent 5,643,570).

Ostberg *et al.* teach a Pharmaceutical composition for treatment of a cytomegalovirus (CMV) viral infection, the composition comprising a buffer (Examples III and IV) and a human anti-CMV antibody which comprisies a human immunoglobulin heavy chain having a variable region of SEQ ID NO:3 and a human immunoglobulin light chain having a variable region of SEQ ID NO:3 (claim 6 of U. S. Patent 5,750,106; claims 53 and 54). However, Ostberg *et al.* do not dislose the use of an adjuvant in the pharmaceutical composition. Theofan *et al.* teach a pharmacutical composition comprising BPI-immnoglobulin fusion protein together with carriers, adjuvants and diluents for treating gram-negative bacterial infections (column 3, lines 36-49). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to include an adjuvant taught by Ostberg *et al.* for preparing the a pharmaceutical composition as taught by Ostberg *et al.* (claim 55) because the use of an adjuvant in the pharmacutical composition would aid the effect of the active agent. Thus, the combined references result in the

claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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January 11, 2003